

## REMARKS

**The Examiner rejected Claims 65-68 and 70-80 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.** Applicant traverses the rejection.

The Examiner stated that there was no support in the specification for the claim wording introduced in the response filed on 12/17/2010 in claim 65 regarding sample descriptive values and measurement descriptive values, and that as such it was found to constitute new matter.

The relevant limitations in claim 65 require that **each sample descriptive value characterize a corresponding sample independent of said measurements**, and that **each measurement descriptive value characterize a corresponding type of measurement or measurement condition, independent of any one of said samples**.

Applicant directs the Examiner's attention to paragraph [0080], which discusses the display of experimental and descriptive data in a single view. The sample descriptive values and measurement descriptive values recited in the claims are two sub-categories of the "descriptive data" discussed. Applicant also directs the Examiner's attention to Figure 2 and associated paragraphs [0084] through [0087] in the specification.

First, the data shown in Row 4 of the display in Figure 2 are examples of sample descriptive values, as they characterize particular samples (in the microarray whose measured data are also shown in the heat maps) on the basis of the gender of the patient whose samples are being tested, "where 'M' symbolizes male, 'F' symbolizes female, and 'U' symbolizes that the sex of the patient was not recorded" (paragraph [0084]). Such clinical or patient data are independent of the measurements subsequently made on the samples in the array.

Second, the data shown in column 43 are examples of measurement descriptive values, as they characterize a corresponding type of measurement condition, the particular "*Unigene Cluster ID that further identifies the CDNA having been deposited on the microarray, with*

*respect to each of the respective cells in each array 1-31. Thus, for example, Unigene Cluster ID 'Hs 23590' is associated with the first row of experimental data 110 as shown in Fig. 2"* (paragraph [0080]). Descriptive data of this type are clearly independent of the samples tested with those particular CDNA probes in the corresponding cells of the array.

Accordingly, Applicant submits that one of skill in the art reading the specification as originally filed would understand the meaning of the terms in question recited in independent claim 65. Hence, claims 65-68 and 70-80 do not include "new matter" and are in compliance with the first paragraph of 35 U.S.C. 112.

**The Examiner rejected Claim 71 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicant submits that as currently amended, claim 71 is not indefinite.**

The Examiner stated that the limitation "positive and negative annotative binary data values" in line 3 had insufficient antecedent basis. The claim has been amended to cure the defect.

**The Examiner rejected Claims 65-67, 69, 75, and 79-80 under 35 U.S.C. 103(a) as being unpatentable over Warrington et al. (P/N 6,884,578; no. 2 reference in IDS submitted 11/6/2008) ("Warrington") in view of Rusterholz (US P/N 5,864,838) ("Rusterholz") in view of Balaban et al. (6,185,561; no. 3 reference submitted in IDS 11/6/2008) ("Balaban'561") and further in view of Tamura et al. (US 2002/0021299) ("Tamura") and further in view of Gruenwald (US P/N 2002/0194176) ("Gruenwald"). Applicant submits that as currently amended, claims 65-67, 75 and 79-80 are not obvious in view of the cited prior art. Applicant presumes the Examiner listed claim 69 in error as the claim has been withdrawn.**

A prima facie case of obviousness has three requirements. First, the prior art relied upon, coupled with the knowledge generally available in the art at the time of the invention, requires some reason that the skilled artisan would modify a reference or to combine references. (See Princeton Biochemicals, Inc. v. Beckman Coulter, Inc., 411 F.3d 1332 (Fed. Cir. 2005), “[S]imply identifying all of the elements in a claim in the prior art does not render a claim obvious.”) The Supreme Court has, however, cautioned against the use of “rigid and mandatory formulas” particularly with regards to finding reasons prompting a person of ordinary skill in the art to combine elements in the way the claimed new invention does. (See KSR Int’l Co. v. Teleflex Inc., 127 S. Ct. 1727 (2007), “The obviousness analysis cannot be confined by a formalistic conception of the words teaching, suggestion, and motivation, or by overemphasis on the importance of published articles and the explicit content of issued patents.”) But rather the Supreme Court suggests a broad, flexible “functional approach” to the obviousness analysis recognizing that “[i]n many fields it may be that there is little discussion of obvious techniques or combinations.” (Id. See also Id. at 1743 F. 3d 1356 (Fed. Cir. 2006), “Our suggestion test is in actuality quite flexible and not only permits, but requires, consideration of common knowledge and common sense.”) Second, the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the same time the invention was made. In other words, a hindsight analysis is not allowed. (See Amgen, Inc. v. Chugai Pharm. Co., 927 F.2d 1200 (Fed. Cir. 1991), “Hindsight is not a justifiable basis on which to find that ultimate achievement of a long sought and difficult scientific goal was obvious.”) Lastly, the prior art reference or combination of references must teach or suggest all the limitations of the claims. (See In re Wilson, 424 F.2d 1382 (C.C.P.A. 1970), “All words in a claim must be considered in judging the patentability of that claim against the prior art.”)

If there is no suggestion to combine the teachings of the applied art, other than the use of Applicants’ invention as a template for its own reconstruction, a rejection for obviousness is improper. (Ex parte Crawford, et al. Appeal 20062429, May 30, 2007.) In furtherance to the need for the suggestion to combine the teachings of the applied art, it is established that rejections on obviousness grounds cannot be sustained by mere conclusory statements: instead

there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness. (KSR Int'l v. Teleflex, 127 S. Ct. at 1741.)

The Examiner states that Warrington teaches all the limitations of claim 65 except for (1) **calculating a pseudo-data vector** and (2) **reordering said data matrix based on a measure of similarity of values** corresponding to one of said samples or physical measurements. The Examiner looks to Gruenwald as providing teaching (1) and to the combination of Rusterholz, Balaban'561 and Tamara as providing teaching (2).

First, claim 65 has been amended to explicitly specify that the pseudo-data vector be calculated from the plurality of sample descriptive values or from the plurality of measurement descriptive values, independent of the measured values representing said physical measurements. The written description of the originally filed specification supports this limitation in numerous places, beginning with the following statement in paragraph [0012]: *"A pseudo-data vector may be calculated from data that is descriptive of the dataset being examined, but not part of the actual data in the dataset."*

Gruenwald discloses data vectors representing "*raw data*" in numeric or alphanumeric form. There is no teaching in Gruenwald that the data are limited to sample descriptive values or measurement descriptive values as recited in the amended claim. There is no such teaching in any of the other cited references. Hence, the limitation regarding the calculation of the pseudo-data vector as recited in claim 65 is not provided in the cited prior art.

Second, the Examiner maintains that Warrington describes at column 14, lines 32-48, lines 61-67, and column 15, lines 30-47 that this data can be analyzed by software and interacted with using a graphical user interface to identify patterns and variation. Applicant must respectfully disagree with the Examiner's reading of the passages in question. These passages discuss the type of data that may be included such as expression profiles from microarrays and the usefulness in analyzing experimental samples from females. However, there is no mention of any **graphical display**, no less one that meets the display limitation of Claim 65. The Examiner



also argues that since Warrington at column 13, lines 54-58 describes an illustrated example of a computer system that may be used to execute the software of an embodiment of the invention, wherein the system comprises a display, it is inherent that Warrington teach a display used for displaying the tables of data and results of the analysis and data manipulation steps, etc.

At most, the cited passages teach that a data analysis system can be run on a general-purpose computer having a mouse and display. Such a display can be used for many types of interactions, including displays that are not two-dimensional detail displays having a plurality of cells, each cell corresponding to one of said values in said data matrix, said display providing a view of a portion of said data matrix that is defined by a base location in said data matrix. Hence, this limitation is not inherent. Accordingly, Applicant submits that Warrington does not teach the required display.

The Examiner admits that Warrington does not teach the reordering operations required by the claim. The Examiner attempts to overcome this lack of teaching by first, stating that Warrington teaches a relational database and that it is an inherent property of a relational database that rows or columns can be sorted based on varying criteria or rules created by the designer. The issue is not whether rows and columns can be sorted, but rather whether there is a teaching that would cause the two-dimensional display to be reordered based on the recited similarity measure when the user picks a cell from a view showing a portion of the table followed by the display of a different portion of the database.

The Examiner looks to Rusterholz (abstract, column 4, lines 55-67 through column 8) as teaching “*rearranging tables of data and a reordering module designed to reorder the data in different ways, such as by user input and using “pseudo-data vectors,” i.e. arrays wherein the vector data is used for reordering*”. In addition, the Examiner points to Balaban’561 as teaching the extraction of rows based on a query that extracts all columns with a value greater than a predetermined value for some entry in the column. The Examiner asserts that this results in a reordering of the data, and that hence, the data mining taught by Balaban’561 “*incorporates the capability of sorting and reordering the expression data as it is a common goal of any data*

*mining to be able to sort and reorder data*". Again, the Examiner's argument is basically that a database program can reorder and data extract in response to queries.

The Examiner also points to Gruenwald [0009] - [0012] as teaching known methods of organizing data in a database, involving sorting data vectors. Merely sorting data vectors is not equivalent to the sorting of matrix data based on a similarity measure (or any other measure) determined **by** the measured matrix data being sorted **and** by another vector, let alone the pseudo-data vector recited in the claim.

Finally, the Examiner looks to Tamura as teaching the display of data that have been reordered based on similarity scores, specifically pointing to Figures 7-9 and paragraphs [0017]-[0019]. The issue is not whether reordering of a table based on a similarity measure is known. The claim requires a very specific type of reordering based on a measure of similarity of values corresponding to one of said samples or physical measurements that is picked by the user by pointing to a cell in the display. This type of interactive display is not taught in any of the references. The cited passages in Tamura concern similarity scores and patterns between probes, for example the similarity score "*between specific one of the probe biopolymers and each of the probe biopolymers*". Such a similarity measure is clearly not determined by similarity between **measured data values** in a matrix and **another vector**, let alone the pseudo-data vector recited in the claim.

Accordingly, Applicant submits that claim 65 and the claims dependent therefrom are not obvious in view of the cited prior art.

Claim 66 depends from claim 65 and additionally requires that the pseudo-data vector be generated by assigning numerical data values to a selected portion of the sample descriptive values. The Examiner points to Balaban'561 at columns 3 and 5 teaching the use of queries comprising numerical data values, and to Tamura as teaching reordering data based on numerical data values. However, neither teaches the **assignment** of numerical data values **to** a selected portion of **sample descriptive values** as recited. Hence, there are additional grounds for allowing

claim 66 and the claims dependent therefrom.

Claim 67 depends from claim 66 and additionally requires that said selected sample descriptive values to which numerical data values are assigned comprise binary data. The Examiner points to column 5 of Rusterholz as providing this teaching. The binary data disclosed in the cited column are new and old index bit sequences. First, these sequences cannot be interpreted to be sample descriptive values as recited, as they simply indicate the addresses of particular data items in the database. Second, although these sequences may comprise binary data, there is no teaching that numerical data values are assigned to these sequences. The issue is not whether it is obvious to represent data in binary form but whether the specific assignment recited in the claims with regard to **sample descriptive values** would have been obvious. The teachings of Rusterholz are irrelevant in this regard. Hence, there are additional grounds for allowing claim 67.

**The Examiner rejected claims 68, 70-72, and 76-78 under 35 U.S.C. 103(a) as being unpatentable over Warrington in view of Rusterholz in view of Balaban'561 in view of Tamura and further in view of Gruenwald as applied to claims 65-67, 69, 75, and 79-80 above and further in view of Balaban et al. (US A/N 2003/0028501) ('Balaban'501') and further in view of Warrington (US 2003/0124539) ('Warrington'539'). Applicant submits that as currently amended, claims 68, 70-72, and 76-78 are not obvious in view of the cited prior art.**

The Examiner states that the combination of Warrington, Rusterholz, Balaban'561, Tamura and Gruenwald teaches the limitations of claims 68, 70-72, and 76-78 except for the additional limitations over the base claim 65 regarding details of the data display. .

Claim 68 depends from claim 66 and additionally requires cells of said selected sample descriptive values be color-coded, said color-coding representing a function of the sample descriptive values in the cells. The Examiner looks to Balaban '501 and Tamura for the additional teachings. The Examiner maintains that it would have been obvious to apply the teachings of Balaban'501 to those of Warrington, modified by Rusterholz, Balaban'561, and

Gruenwald “*because using color as a way of displaying and manipulating data is recognized by Balaban et al. (‘501) and Tamura as a functionality used in data manipulation and displays*”.

As noted above, the combination of Warrington, Rusterholz, Balaban‘561 and Gruenwald fails to teach either the requirements of claim 65 (regarding the calculation of the pseudo-data vector, the reordering of a data matrix **based on a measure of similarity between** the pseudo-data vector and measured values of said data matrix, and the recited data display) or the additional requirements of claim 66 (requiring that the pseudo-data vector be calculated by assigning numerical data values to a selected portion of the sample descriptive values). Balaban‘501 does not provide the missing teachings. Hence, claim 68 and the claims dependent therefrom are not obvious in view of the cited prior art.

Claim 70 depends from claim 66 through claim 68 and additionally requires that at least one cell of said data matrix lack a sample descriptive value, and wherein said calculation of said pseudo-data vector further comprises **assigning a predefined null value to said cell lacking a sample descriptive value**. First, as noted above with respect to claim 68, the cited prior art does not teach the limitations of base claim 66. Second, Applicant finds no teaching in the cited paragraphs or elsewhere in Balaban‘501 that an assignment of any value is made **to a cell lacking a sample descriptive value**. Third, there is no teaching that any of the annotations made by the user of Balaban‘501 is “*a preset null or negative value*” as the Examiner asserts. At most, paragraph 0071 of Balaban‘501 teaches that annotations added to the display may include text, a user-defined type of the annotation, user name, date, or “other useful information”.

In the current office action, the Examiner points to paragraphs [0006] and [0008] of Warrington‘539 as teaching the assignment of null values to “data representing sample descriptive data”. The cited passages discuss the calculation of likelihood values for forward and reverse strands using five different homozygote models, but Applicant finds no teaching regarding any null values or of cells including or lacking sample descriptive data. Hence, there are additional grounds for allowing claim 70.

Claim 71 depends from claim 67 and additionally requires that said assigning numerical



data values to a selected portion of said sample descriptive values comprise **substituting predefined pseudo-data values for positive and negative annotative binary data values** in said selected portion of said sample descriptive values. First, as noted above, the combination of Warrington, Rusterholz, Balaban'561, Tamura and Gruenwald does not teach the limitations of base claim 67. Balaban'501 and Warrington'539 do not provide the missing teachings. Second, the passages cited by the Examiner in Balaban'501 do not mention **substituting** any values for values that are already present, or even "*equating*" such values as the Examiner asserts, let alone that the values being replaced are positive and negative annotative binary data values. Hence, claim 71 is not obvious in view of the cited prior art.

Claim 72 depends from claim 66 and additionally requires that the numerical data values that are assigned to said selected portion of said sample descriptive values be inverted. As noted above, the combination of Warrington, Rusterholz, Balaban'561, Tamura and Gruenwald does not teach the limitations of base claim 66. Balaban'501 and Warrington'539 do not provide the missing teachings. In the current office action, the Examiner points to Rusterholz (Fig. 6) as teaching that "inverting the data is a known technique used by the skilled artisan for data manipulation". The issue is not whether this particular technique is well known, but whether it would have been obvious to apply it to the data of the modified primary reference. The Examiner has not pointed to any motivation for such an application. Hence, Applicant maintains that claim 72 is not obvious in view of the cited prior art.

Claim 76 depends from claim 65 and additionally requires that said assigning numerical data values to a selected portion of said sample descriptive values comprise **substituting** a first predefined pseudo-data value for emphasizing each cell in a sub-portion of said selected portion of said sample descriptive values, and a second predefined pseudo-data value for de-emphasizing each remaining cell of said selected portion of said sample descriptive values. First, as noted above, the combination of Warrington, Rusterholz, Balaban'561, Tamura and Gruenwald does not teach the limitations of base claim 65. Balaban'501 and Warrington'539 do not provide the missing teachings. Second, as noted above with respect to claim 71, the cited prior art does not teach **any** substitution of one value for another, let alone the specific type of substitutions recited

in claim 76. Hence, claim 76 and the claims dependent therefrom are not obvious in view of the cited prior art.

Claim 77 depends from claim 76 and additionally requires that said first predefined pseudo-data value for emphasizing be a positive value inputted by a user. As noted above with respect to claim 70, at most, Balaban'501 teaches (paragraph 0071) that annotations added to the display may include text, a user-defined type of the annotation, user name, date, or "other useful information". There is no teaching that the user inputs a positive value as recited. Hence, there are additional grounds for allowing claim 77.

In the current office action, with regard to the rejections of claims 70-72 and 76-78, the Examiner points to Gruenwald as teaching (paragraph [0122]) *"filtering based on positive and negative relationships, which reads on data that emphasizes and/or de-emphasizes values"*. First, Gruenwald does not include a paragraph [0122]. Applicant has searched without success to find another paragraph in Gruenwald that teaches the "filtering" cited by the Examiner. Moreover, the issue is not whether it is known to emphasize or de-emphasize data values in a matrix, but whether the particular actions related to such emphasizing or de-emphasizing recited in these claims are either taught or made obvious by the cited prior art. Applicant maintains that they are not.

**The Examiner rejected claims 73-74 under 35 U.S.C. 103(a) as being unpatentable over Warrington in view of Rusterholz in view of Balaban'561 and further in view of Tamura and further in view of Gruenwald as applied to 65-67, 69, 75, and 79-80 above and further in view of Schadt et al. (US P/N 7,035,739) ("Schadt"). Applicant submits that as currently amended, claims 73-74 are not obvious in view of the cited prior art.**

Claim 73 depends from claim 65 and additionally requires that said measure of similarity comprise calculating a distance value between the pseudo-data vector and a vector generated from a select set of said measured values. Claim 74 depends from claim 73 and additionally requires that said distance value be determined by calculating a squared Euclidean distance

between said two vectors.

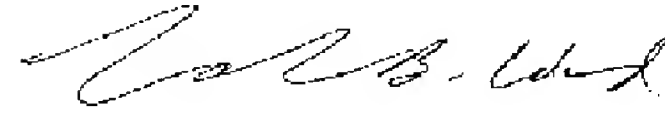
The Examiner states that the combination of Warrington, Rusterholz, Balaban`561, and Tamura and Gruenwald teaches the limitations of claims 73 and 74 except for calculating a distance value between rows assigned a similarity value wherein the calculation is a Euclidean distance. The Examiner maintains that measures of similarity based on distance values including a squared Euclidean distance are known measures of similarity, as evidenced by Schadt, and hence, it would be obvious to use these measures in data re-ordering. The Examiner also points to column 27 of Warrington as providing further support for this position, discussing the computer package GeneCluster. Applicant assumes the Examiner intended to cite column 25 in this regard (there is no column 27).

First, as noted above, the combination of Warrington, Rusterholz, Balaban`561, and Tamura and Gruenwald does not teach the limitations of base claim 65. Schadt does not provide the missing teachings.

Second, Schadt teaches a clustering algorithm. The fact that certain measures of distance are known in clustering theory does not make those measures obvious as criteria for ordering records of a database. The teachings of Warrington cited above are irrelevant in this regard. Accordingly, Applicant submits that claims 73 and 74 are not obvious in view of the cited prior art.

Applicant submits that all claim amendments presented herein or previously are made solely in the interest of expediting allowance of the claims and should not be interpreted as acquiescence to any rejections or ground of unpatentability. Applicant reserves the right to file at least one continuing application to pursue any subject matter that is canceled or removed from prosecution due to the amendments.

Respectfully Submitted,

A handwritten signature in black ink, appearing to read "Calvin B. Ward".

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